Development of Different Natural Polymeric Biocompatible Materials for Wound Healing

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An injury or wound results in disruption of healthy tissues as well as a breakdown in the skin's protective layer. Replacing damaged skin or other tissues is a dynamic and intricate phenomena known as wound healing. On the basis of the recovery period, the wounds are differentiated into acute and chronic wounds. According to WHO annually maximum mortality rates are induced by burn wounds associated with the growth of various types of pathogenic bacteria and form sepsis. Therefore, various reports suggested that wound dressing or wound care management is the most important for fast wound recovery, reduced wound infection, and subsequently decreased mortality rates. In the last decades, various forms of wound healing materials have developed like hydrogel, nanoparticles, mesosphere, scaffold, ointment, etc., and most of the materials were synthesized from either chemical or natural processes. The naturally synthesized materials are usually high prices and produced very low amounts. In this thesis, we have formulated three types of biocompatible, biodegradable, and cheap-priced skin wound care management products and tested them against acute and chronic wounds.

Firstly, we fabricated polyherbal extract (*Hibiscus rosa-sinensis and Calendula officinalis* flower extract) encapsulated xanthan gum hydrogel matrix (X@C-H) and applied in excision wound. During ancient times, the tribal communities utilized the *Hibiscus rosa-sinensis* and *Calendula officinalis* flowers as herbal remedies for a wide range of health conditions. However, the herbal medicines loading and delivery are significantly tricky process due to the maintenance of their molecular structure against some environmental factors like moisture, temperature, plus other ambient factors. Our synthesized polyherbal extract was phytochemically screened, which revealed the presence of several compounds including alkaloids, flavonoids, terpenoids, saponins, tannins, glycosides, anthraquinones, a few percentages of reducing sugar and amino acids. The polyherbal extract encapsulated xanthan gum hydrogel matrix released the polyherbal extract slowly for extended time. When tried in in-vitro system, the X@C-H significantly improved the proliferation and migration of human fibroblast and keratinocyte cells compare to undoped excipient treated cells as determined by MTT assay, scratch wound assay, and BrdU assay. Also, the X@C-H treated cells enhanced the expression of the pAkt protein indicating the activation of PI3K signaling pathway. In an in-vivo study, we also noticed that X@C-H treated excision wound-formed male BALB/c murine model resulted reduction in wound area within the 12^{th} day and helped for re-epithelization, granulation process compared to the other groups (untreated, X, X@C, X@H). As a result, we believe that this biocompatible hydrogel could serve as a potential transporter for herbal excipients.

Additionally, we formulated a mucilage polymer (HM) from the leaves of *Hibiscus rosa sinensis* and its potential utilization in the treatment of second-degree burn and excision wounds has been assessed. Mucilage is a sticky material found in diverse plant species and microorganisms, composed of protein and polysaccharides. Due to its stabilizing, emulsifying, moisturizing, and soothing characteristics, it finds widespread application in the food sector and skin care products. The in vitro experiment indicates that the addition of HM polymer promotes the migration and proliferation of human lung fibroblasts (WI-38) and keratinocytes (HaCaT) cells. Furthermore, HM polymer exhibits biocompatibility antioxidant, and anti-inflammatory properties. During an in vivo experiment conducted on BALB/c mice with second-degree burn and excision wounds, it has been observed that the HM-treated mice developed hair follicles, new tissue, and also blood vessels within six days and cured the wound within 11^{th} days.

Finally, we focused on antibiotic-resistant bacteria-infected wound infection. Recently various scientists have developed nanoparticle-mediated antibacterial agents but most of the nanoparticles have some toxic effect. Therefore, we have developed green silver nanoparticles encapsulated mucilage microsphere (HMMS@GSNP). Both the silver nanoparticle and the mucilage polymer were obtained from *Hibiscus rosa sinensis* leaves. Microspheres are porous and spherical structures made of a variety of materials, including polymers, glass, ceramics, metals, and more. In

the current study, we have utilized the HMMS@GSNP microsphere as a therapeutic intervention for the treatment of second-degree burns and excision wounds that have been contaminated by pathogenic bacteria. The HMMS@GSNP microsphere released GSNP nanoparticles from their surface through the control release process. This HMMS@GSNP microsphere showed strong antibacterial, cell proliferation, migration, antioxidant, and anti-inflammation activity compared to untreated, GSNP (green silver Nanoparticle) and HMMS (hibiscus mucilage polymer). In in vivo experiment, we observed that the HMMS@GSNP microsphere treated either MRSA infected second-degree burn or MRSA infected excision wound bearing male BALB/c mice =significantly recovered injured area and decreased bacterial infection within 20th days compared to other groups (untreated, Silverex ionic gel, $AgNO_3$, HMMS, GSNP). Thus, the HMM@GSNP microsphere is an excellent therapeutic material that can be used as a topical agent for the management of chronic wound therapy.

Moreover, our all data suggested that our synthesized X@C-H hydrogel matrix, HM polymer, and HMMS@GSNP microsphere are suitable for acute or chronic wound-healing agents and other biomedical applications for the near future

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